

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES**

In re Patent Application of
Saidi, Zahir et al.

Application Serial No.: 10/019,100

Filed: August 21, 2003

For: AQUEOUS COMPOSITIONS CONTAINING
CORTICOSTEROIDS FOR NASAL AND
PULMONARY DELIVERY

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RESPONSE TO EXAMINER'S REPLY BRIEF

Sir:

Appellants submit this Response to the Examiner's Reply Brief (*Examiner's Reply*) of
April 15, 2010, in furtherance of the Appeal Brief filed on March 2, 2010.

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II. TABLE OF AUTHORITIES

Statutes

35 U.S.C. § 103

Rules and Regulations

MPEP § 2141.02

Cases

In re Wesslau, 353 F.2d 238, 241 (CCPA 1965)

In re Fine, 837 F.2d 1071, 1075, 5 U.S.P.Q.2D (BNA) 1596 (Fed. Cir. 1988)

In re Mercier, 515 F.2d 1161, 1166, 185 U.S.P.Q. (BNA) 774, 778 (CCPA 1975)

BAUSCH & LOMB, INC. v. BARNES-HIND/HYDROCURVE, INC. and BARNES-HIND INTERNATIONAL, INC., 796 F.2d 443, 449 (Fed. Cir. 1986)

III. STATUS OF CLAIMS

Currently, claims 1-6 and 8-18 are under consideration. The status of claims 1, 4, 5, 8-11, and 18 is "Previously Presented." The status of claims 2, 3, 6, 12-17 is "Original." Each of these claims has been rejected.

IV. GROUNDS OF REJECTIONS TO BE REVIEWED.

Previously, Appellants asked the board to review two grounds of rejection: a rejection based on § 103 and a rejection based on obviousness-type double-patenting. In the Examiner's Reply, the Examiner has withdrawn the obviousness-type double-patenting rejection. Accordingly, the sole ground for rejection is whether the Examiner erred in concluding that claims 1, 6, 10, 13-17, and 22-27 are obvious under 35 U.S.C. § 103 in view of US Patent 6,193,985 to Sonne.

V. ARGUMENT

In the Examiner's answer, the Examiner dismissed the Appellants' analysis provided in the original Appeal Brief without any analysis as to why the Appellants' arguments are flawed. Instead, the Examiner simply re-iterated an excerpt from Sonne that Sonne discloses embodiments where the active ingredient is dissolved in tocopherol or a derivative thereof and where tocopherol or a derivative thereof may be used as a solvent and/or emulsifier for sparingly water-soluble drugs.

Appellants respectfully maintain that separate grounds for patentability exist for each of the following groups of claims: (a) claims 1, 6, 10, 16, and 22-25 stand and fall together, (b) claims 13, 14, 15, 26, and 27 stand and fall together, and (c) claim 17 stands and falls independently of the other claims (noting that claims 1, 15, 16, and 17 are independent claims). Appellants present their arguments according to the grouping of claims.

1. Claims 1, 6, 10, 16, and 22-25.

The Examiner's position is inconsistent with the teachings of Sonne for multiple reasons provided in the original Appeal Brief and further explained herein.

a. Removal of an element and retention of its function is indicia of non-obviousness.

Independent claims 1 and 16 recite the transition phrase "consisting of" and include the limitation that "said ethoxylated derivative of vitamin E is the sole vitamin E component in the composition." In contrast, Sonne's compositions must have tocopherol or a derivative thereof which is not Vitamin E TPGS.

Appellants respectfully note that it has been well-settled law that the omission of an element and retention of its function is an indicia of nonobviousness. See *In re Edge*, 359 F.2d 896, 149 USPQ 556 (CCPA 1966).

In this case, it is unarguable that the instant claims exclude Sonne's solvents, while the function of these compounds (which is to dissolve the active agent) is retained: the active agent is still dissolved and useful emulsions are formed.

b. Sonne defines vitamin E-TPGS as a tocopherol derivative emulsifier, not as a tocopherol derivative solvent – clearly distinguishing those functionalities.

In the final rejection, the Examiner argues that it would be obvious to remove Sonne's solvents and use Vitamin E TPGS both as the solvent and the emulsifier. The Examiner's argument is built on two portions of Sonne.

First, the Examiner argues that Sonne, in *Col. 6, lns 18-23* refers to embodiments where the active ingredient is dissolved in tocopherol or a derivative thereof.

Second, the Examiner argues that Sonne discloses that tocopherol or a derivative thereof may be used as a solvent and/or emulsifier for sparingly water-soluble drugs. *Sonne, Abstract*.

Appellants respectfully submit that Examiner takes these portions out of context, thereby acting contrary to MPEP § 2141.02 and case law. It is well settled law that the prior art references should be considered as a whole. "It is impermissible within the framework of section 103 to pick and choose from any one reference only so much of it as will support a given position, to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one of ordinary skill in the art". *In re Wesslau*, 353 F.2d 238, 241 (CCPA 1965). Contrary to that legal principle, the Examiner analyzes Sonne by picking and choosing certain portions of the disclosure out of context. Further, even though these portions may be

interpreted in several ways, without any reason whatsoever the Examiner provides only one interpretation and does not consider any other interpretations of these portions.

Regarding the two excerpts relied upon by the Examiner, the phrase “the use of a tocopherol or a derivative thereof as a solvent and/or emulsifier” does not necessarily mean that the same derivative of tocopherol is or can be used as a solvent and an emulsifier. Interpreting this phrase in a vacuum, this phrase may mean that one tocopherol derivative is used as a solvent while another derivative is used as an emulsifier. This phrase may also mean that tocopherol itself is a solvent, while a derivative of tocopherol is an emulsifier. The Examiner does not address these possible alternative interpretations, and instead, without any logical reasoning, selects only the interpretation which appears to support her position, notwithstanding what one of ordinary skill in the art would understand Sonne to teach. In view of the ambiguous meaning of the statement relied upon by the Examiner, inquiry into the rest of Sonne's disclosure is warranted.

When Sonne is considered as a whole, the limited teaching relied upon by the Examiner is insufficient for concluding that Sonne fairly teaches or suggests that Vitamin E TPGS is suitable for using as both solvent and emulsifier. While on its face Vitamin E is a derivative of tocopherol, Sonne's disclosure does not teach or suggest that vitamin E TPGS is a derivative that is also suitable as a solvent.

To the contrary, when Sonne is read as a whole, its implicit teaching is that vitamin E TPGS is to be used as an emulsifier only. For example, throughout the disclosure, vitamin E TPGS is explicitly separated from tocopherol and other derivatives thereof. While vitamin E and derivatives thereof, such as acetate, linoleate, nicotinate or hemi-succinate are disclosed only as

solvents (but never mentioned as emulsifiers), vitamin E TPGS, in contrast, is disclosed only as an emulsifier (not a solvent).

Appellants submit at least seven instances of Sonne's express distinction made between vitamin E TPGS and other tocopherol derivatives: claim 1, claim 11, claim 22 (all of the claims discussing tocopherol or acetate, linoleate, nicotinate or hemi-succinate derivative thereof as solvents in one phase of the composition and Vitamin E TPGS as an emulsifier, present in a different phase of the composition), *Col. 4 lns 41-49* ("composition suitable for delivery of substantially insoluble or sparingly soluble biologically active agents, comprising a tocopherol or a derivative thereof, and Vitamin E TPGS as emulsifier" and "Stable emulsions may readily be achieved according to the invention using a range of tocopherols or derivative compounds as solvents, with Vitamin E TPGS as emulsifier, and any suitable aqueous medium"), *Col. 5, ln 65-Col. 6, ln 2* ("active ingredient can be dissolved in the lipid fraction of the tocopherol solvent and other solvents may be added if desired. The emulsifier, eg. Vitamin E TPGS, and optionally other emulsifiers, can be added to either the oil and/or the water phase"), *Col. 6, lns 18-28* (analyzed above).

Sonne further discloses lists of suitable solvents and suitable emulsifiers. The lists of suitable solvents and emulsifiers do not overlap. Therefore, one of ordinary skill in the art would understand from Sonne that Sonne distinguished between emulsifiers and solvents, which are not art-recognized equivalents, and therefore, are not interchangeable.

By virtue of being an inventor, Sonne's level in the art is above ordinary (see *BAUSCH & LOMB, INC. v. BARNES-HIND/HYDROCURVE, INC.* and *BARNES-HIND INTERNATIONAL, INC.*, 796 F.2d 443, 449 (Fed. Cir. 1986) stating that "Inventors, as a class, according to the concepts underlying the Constitution and the statutes that have created the patent system, possess

something -- call it what you will -- which sets them apart from the workers of *ordinary skill*", emphasis in the original). Thus, if the mental leap made by the Appellant was not obvious to one having above-ordinary skill in the art, it follows that such mental leap would not have been obvious to one of ordinary skill in the art.

If, as the Examiner asserts, it would be obvious to remove the solvent of Sonne and replace it with Vitamin E TPGS, then why did Sonne not disclose it? Why did Sonne clearly separate Vitamin E TPGS from tocopherol derivative solvents not once, not twice, but seven times? There can be only one answer to these questions: considering the disclosure as a whole, Sonne identified Vitamin E TPGS as an emulsifier only because he did not think that Vitamin E TPGS may also be a solvent.

c. There is no reasonable expectation of success from Sonne that use of the vitamin E-TPGS emulsifier as a sole vitamin E compound is sufficient to administer insoluble drugs in a stable emulsion.

The Examiner has not provided any evidence that a person of the ordinary skill in the art would have a reasonable expectation of producing an emulsion of a poorly water soluble drug without a hydrophobic tocopherol-based solvent, as disclosed in Sonne. The only basis for her conclusion is that, as discussed above, Sonne discloses that a tocopherol derivative may be used as a solvent and/or emulsifier and that Vitamin E TPGS is a derivative of tocopherol. However, Appellants respectfully re-iterate that Sonne neither discloses nor suggests that Vitamin E TPGS is a suitable solvent. In fact, Sonne clearly contrasts solvents and emulsifiers in general. Moreover, Sonne explicitly contrasts Vitamin E TPGS from other tocopherol derivatives, as discussed above.

The Examiner concludes that there is "a reasonable expectation of successfully producing a composition that is non-irritating with optimized bioadhesion, sprayability, viscosity, without

compromising the stability of the emulsion,” but this is not the issue at hand. The issue is not whether this composition may be produced, but whether a person of skill in the art would have a reason to produce the claimed invention from the cited references. As discussed above, Sonne clearly distinguishes solvents and emulsifiers, thus teaching that these two functionalities are not interchangeable. The proper analysis of Sonne leads to a conclusion that Sonne teaches that Vitamin E is a suitable emulsifier, rather than a suitable solvent. Accordingly, from the disclosure of Sonne, it appears that if a composition is to be successfully produced, it must contain both tocopherol or a derivative thereof (not Vitamin E TPGS) and Vitamin E TPGS. Thus, one of skill in the art would not have a reason to exclude a solvent α -tocopherol from the compositions of Sonne, and to replace it with an emulsifier, in order to arrive at the compositions of the instant invention. In other words, it is unlikely that one of skill in the art would have reasonably guessed that the solution of a water-insoluble compound in a hydrophobic solvent would be “optimized” by removing the solvent. Accordingly, Appellants respectfully submit that Sonne does not provide a reasonable expectation of producing a stable emulsion of a water-insoluble drug where Vitamin E TPGS is the solve Vitamin E compound..

d. Replacement of tocopherol with Vitamin E TPGS in the composition of Sonne is not routine experimentation because Sonne never disclosed the basic conditions of the instant claims.

As discussed above, Sonne does not suggest removal of an α -tocopherol based solvent from his compositions. The Examiner attempts to overcome this deficiency by arguing that the instant composition could be produced by routine experimentation with concentrations of different compounds in Sonne's composition. Appellants respectfully disagree. Experimentation is routine only when prior art discloses basic conditions of a claim. See, e.g., *In*

re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). Otherwise, just about every experimental procedure may be considered routine.

In this case, the general conditions of the claim are not disclosed by Sonne. In each example of Sonne that disclosed both Vitamin E TPGS and α -tocopherol, the amount of the former was less than the amount of the latter. Thus, the amount of Sonne's tocopherol based solvents is not relatively close to zero. Suggesting otherwise and considering that the amount of Vitamin E TPGS is less than the amount of tocopherol-based solvent, leads to a conclusion that, if anything, Sonne disclosed the composition without Vitamin E TPGS, thus making Sonne even less relevant to the instant claims.

Therefore, Appellants respectfully submit that experimentation leading to compositions which have no tocopherol or other tocopherol-based solvents, except Vitamin E TPGS, is beyond routine. Thus, for at least these reasons, claims 1, 6, 10, 16, and 22-25 are not obvious in view of Sonne.

2. Claims 13, 14, 15, 26, and 27.

Claim 15 is the independent claim of the group. Similarly to independent claims 1 and 16, claim 15 requires that the "ethoxylated derivative of vitamin E is the sole vitamin E component of the composition." Therefore, the reasons of non-obviousness of claims 1 and 16 discussed above are applicable to non-obviousness of claim 15.

Claim 15 also discloses certain co-solvents. Sonne discloses the use of co-solvents, such as "[v]egetable oils such as sesame- or olive- or fractionated coconut oil, alcohols such as ethanol, propylene glycol, glycerol, polyethylene glycol or benzyl alcohol; or triacetin." Sonne, Col 6, lns 51-53. However, Sonne does not disclose or suggest replacement of a tocopherol-based solvent with one of these co-solvents. The prefix "co-" as in "co-solvents" assumes that

these solvents act together with other solvents. Thus, these solvents must act together with something else.

Sonne teaches adding either emulsifier such as Vitamin E TPGS, or co-solvents. Regardless of which alternative is selected, the composition still must contain α -tocopherol. In addition, all formulations according to the invention of Sonne contain an α -tocopherol based solvent, and Vitamin E TPGS is not among those solvents.

Appellants further respectfully assert that for the reasons above, the replacement of tocopherol-based solvent with one or more of the aforementioned co-solvents should not be considered routine experimentation. Finally, as argued above, the instantly claimed compositions lack Sonne's tocopherol-based solvents and yet retain desirable properties conferred by those solvents. Therefore, for these reasons, claim 15 and claims 13, 14, 26 and 27 dependent therefrom, are not obvious in view of Sonne.

3. Claim 17

Similarly to independent claims 1 and 16, claim 17 requires that the "ethoxylated derivative of vitamin E is the sole vitamin E component of the composition." Therefore, the reasons of non-obviousness of claims 1 and 16 discussed above are applicable to non-obviousness of claim 17. Claim 17 from about 0.1 to about 3 percent by weight of an oil.

While Sonne discloses that oil may be used, Appellants further respectfully submit that Sonne does not teach replacement of his tocopherol-based solvent with a vegetable oil. Appellants respectfully refer the Board's attention to Sonne Col 2 lns 1-3 stating that "[t]riglycerides such as vegetable oils are generally non-irritant, but usually these oils are too poor as solvents to be of any use." Thus, according to Sonne, replacement of Sonne's tocopherol-based solvents with vegetable oil would not be successful. In fact, Sonne disparages

the use of oils as solvents, thereby directly teaching away from claim 17 and rendering the composition inoperable. See *In re Fulton*, 391 F.3d 1195, 1201, 73 USPQ2d 1141, 1146 (Fed. Cir. 2004), *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984), MPEP § 2145.X.D.

The Examiner asserts that Sonne disparages the use of these co-solvents only in the Background section of the patent, and therefore, does not accord any weight to this teaching away. In response, Appellants respectfully note that teaching away is still teaching away regardless of where in the patent it is disclosed. The fact remains that Sonne discloses vegetable oils only in addition to a tocopherol solvent which is not Vitamin E TPGS. Since there is no disclosure that the tocopherol solvent which is not vitamin E TPGS may be removed altogether, the only thing left is that vegetable oils can be used as solvents, which Sonne clearly disparages. Therefore, for this additional reason, claim 17 is not obvious in view of Sonne.

VI. CONCLUSION

For the foregoing reasons, it is submitted that the Examiner's rejection of claims 1, 5-10, 13-17 and 22-27 as obvious in view of Sonne was erroneous, and reversal of the rejection is respectfully requested.

Appellants request either that the Board render a decision as to the allowability of the claims, or alternatively, that the application be remanded for reconsideration by the Examiner.

Respectfully submitted,

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